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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,033	11/14/2000	Edward James Rozhon	11133-004-999	9130

20583 7590 08/31/2005

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EXAMINER	
MARX, IRENE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 08/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,033	ROZHON ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-38,40,75 and 76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *21-38, 40, and 75-76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 7/20/05 is acknowledged. Claims 21-38, 40, and 75-76 are being considered on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-38, 40, and 75-76 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Davenport *et al.(* Pediatric Pulmonology, S13 Abstract 34, August 16, 1996) taken with Ubillas *et al.*, Masquelier, Wursch and Remington's Pharmaceutical Sciences and applicants' admissions.

Davenport *et al.* teach the oral administration of SP-303, an aqueous soluble proanthocyanidin polymer composition isolated from *Croton* species, at a dose of 20 mg/kg once per day to treat secretory diarrhea in an animal. The reference teaches the mechanism of action of the compound as involving inhibition of fluid accumulation and cAMP-mediated Cl^- - secretion in secretory diarrhea and suggests the wider therapeutic use of this material to humans and other animals in view of the effects demonstrated. See, e.g., Abstract.

Ubillas *et al.* teaches pharmaceutically compositions comprising a therapeutically effective amount of SP-303 an aqueous soluble proanthocyanidin polymer from *Croton lechleri.* The reference teaches these and similar materials are traditionally administered for the treatment of diarrhea and viral infections in conjunction with milk. Milk is not only a pharmaceutically acceptable carrier, but also is known to protect compositions from the action of stomach acid,

because of the natural neutralizing effects of its proteins, for example. See, e.g., page 78, col. 2, last paragraph.

The references differ from the claimed invention in the specific formulations and coatings to be provided. However, from the Ubillas at least it is clear that various formulations are provided in urban health food stores for various therapeutic and prophylactic purposes. In addition, in view of the recognized mechanism of action of proanthocyanidin polymer composition in the intestine to treat diarrhea, one of ordinary skill in the art would have been motivated to formulate SP-303 or similar aqueous soluble proanthocyanidin polymer from *Croton* or *Calophyllum* to protect them from premature degradation and/or inactivation by stomach acid.

Masquelier recognizes that proanthocyanidin may be administered orally in various stable forms that include coatings, for example (See, e.g., col. 6, lines 43-48) and Wursch teaches that related tannin polymers are administered in various forms that protect compositions from the action of stomach acid, including with milk (See, e.g., Example 12) and coated tablets (See, e.g., example 8).

Moreover, at page 16, first full paragraph of the specification, Applicants disclose that method of making the present formulations is well known in the art, with specific reference being made to "Remington's Pharmaceutical Sciences" (See, e.g., pages 150-533 and pages 1585-1593). Slow release compositions are old and well-known in the art, as adequately demonstrated by applicants.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Davenport *et al.* and Ubillas *et al.* by providing compositions of aqueous soluble proanthocyanidins for oral ingestion which are formulated to protect the proanthocyanidins from the stomach environment and that inhibit or neutralize stomach acid or which are slow release formulations according to the teachings of Masquelier and Wursch for functionally and structurally related polymers and of Remington's Pharmaceutical Sciences for pharmaceutical compositions in general, since the references clearly teach that the technology is well known in the art and for the clear benefits to quality of life of providing compositions for treating secretory diarrhea by inhibiting fluid accumulation and cAMP-mediated Cl^- -secretion as demonstrated by Davenport *et al.*.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of sufficient, clear and convincing evidence to the contrary.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant's arguments directed to previous rejections is noted. These rejections are no longer maintained and are irrelevant to the instant rejection.

Regarding the rejection as a whole, applicant has argued and discussed the references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Similarly, applicants argue that none of the secondary references relied upon by the Examiner teach or suggest the enteric coating or slow release composition of an aqueous soluble proanthocyanidin composition such as SP-303 to protect it from the stomach environment. However, "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." In re Merck & Co. Inc, 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986). The test of obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

In the rejection now of record, the Davenport *et al.* reference teaches the oral administration of SP-303 by gavage of an aqueous soluble proanthocyanidin polymer composition isolated from *Croton* species which is administered with sodium bicarbonate. The reference not only specifies the dose to the administered, but treats the same condition, i.e., secretory diarrhea in an animal. Inasmuch as the reference teaches the mechanism of action of the compound, which is active in the intestine and involves inhibition of fluid accumulation and cAMP-mediated Cl^- -secretion in secretory diarrhea, one of ordinary skill in the art would have had compelling motivation to protect the composition from stomach acid and use well known enteric coatings or slow release formulations for this purpose. As recognized by applicants, Davenport *et al.* does protect the aqueous soluble proanthocyanidin composition by

administering it with a bicarbonate carrier, which would at least neutralize stomach acid, and would protect the composition from the acidic stomach environment.

Regarding the treatment of cholera induced diarrhea in Davenport *et al.*, it is noted that claim 35 is directed specifically to this condition.

Applicants have not overcome the strong *prima facie* case made over the references. Therefore the rejection is deemed proper and it is adhered to.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx
Primary Examiner
Art Unit 1651